BIRTH DEFECT RISK FACTOR SERIES: HYDROCEPHALY

DEFINITION

Congenital hydrocephaly is one of the most common central nervous system anomalies. Hydrocephaly is an enlargement of the head caused by an abnormal accumulation of cerebrospinal fluid (CSF) in the cranium due to an imbalance between the production and absorption of CSF. This forces the ventricles to enlarge (ventricular dilatation or ventriculomegaly), which in turn exerts pressure on the surrounding brain tissue, causing the brain tissue to shrink and the head to enlarge (Schrander-Stumpel and Fryns, 1998; Buyse, 1990; Vintzileos et al., 1983). Congenital hydrocephaly usually develops by the twentieth week of gestation (Stoll et al., 1992a).

There are various types or classifications of congenital hydrocephaly. Aqueductal stenosis is a type of hydrocephaly which results from narrowing of the aqueduct of Sylvius, an opening connecting the third and fourth ventricles in the brain. It is the most common form of hydrocephaly. Dandy-Walker syndrome is a group of defects consisting of enlargement of the fourth ventricle of the brain, complete or partial absence of the cerebellar vermis (the middle area between the two cerebral hemispheres), cyst of the posterior fossa (internal base of the skull), and hydrocephaly. The hydrocephaly associated with Dandy-Walker syndrome may not be present at birth but develop later (Buyse, 1990). Dandy-Walker syndrome accounts for 5-12% of hydrocephaly (Vintzileos et al., 1983).

Congenital hydrocephaly is heterogeneous in origin. The defect can be associated with chromosomal abnormalities (trisomy 21, trisomy 13, trisomy 18, triploidy, etc.) and other syndromes (Walker-Wardburg syndrome, Meckel syndrome, Smith-Lemli-Opitz syndrome, and chondrodystrophies, etc.). Some cases seem to be linked to the X chromosome (Torfs and Christianson, 1998). About one-quarter of the infants with hydrocephaly also have spina bifida; conversely, approximately 80% of children with spina bifida also have hydrocephaly. Hydrocephaly can also be secondary to central nervous system anomalies (encephalocele, holoprosencephaly, neoplasms, etc.). Most congenital hydrocephaly cases have additional birth defects such as congenital heart disease and cleft lip and/or palate (Schrander-Stumpel and Fryns, 1998; Stoll et al., 1992a; Buyse, 1990; Drugan et al., 1989; Hudgins et al., 1988; Vintzileos et al., 1983; Chervenak et al., 1985).

Hydrocephaly (ventriculomegaly) can be detected prenatally by ultrasonography (Fadel, 1989; Vinzileos et al., 1987). Studies from various birth defects surveillance systems have found that, in regions where elective termination is allowed, prenatal diagnosis and elective termination reduce the birth prevalence of congenital hydrocephaly (Riley et al., 1998; Julian-Reynier et al., 1994; Stoll et al., 1995; Stoll et al., 1992a; Stoll et al., 1992b; Stone et al., 1989; Drugan et al., 1989; Hudgins et al., 1988; Chervenak et al., 1985).

DEMOGRAPHIC AND REPRODUCTIVE FACTORS

One study reported **racial/ethnic** differences in hydrocephaly rates, with the rate being highest for Native Americans, followed by African-Americans, whites, Asians, and Hispanics (Chavez et al., 1988). Another study found hydrocephaly risk to be lower among infants of Vietnamese mothers when compared with infants of non-Hispanic white mothers (Shaw et al., 2002). However, other investigations did not identify any racial/ethnic differences in hydrocephaly risk (Leck and Lancashire, 1995; Stoll et al., 1992a; Wiswell et al., 1990; Finley et al., 1980).

A **secular trend** for congenital hydrocephaly has been reported by one study, where a decline in prevalence over time was found, paralleling the decline in neural tube defect prevalence (Stone et al.,

1989). However, another investigation observed no trend (Wiswell et al., 1990). There does not appear to be any **seasonal variation** in congenital hydrocephaly prevalence (Stoll et al., 1992a; Castilla et al., 1990; Wiswell et al., 1990; Bound et al., 1989).

Congenital hydrocephaly prevalence does not appear to be influenced by **geographic location** (Stoll et al., 1992a). However, one study found a reduction in hydrocephaly risk with **higher altitudes** (Castilla et al., 1999).

Parental age does not clearly seem to affect risk of having a child with hydrocephaly (Hollier et al., 2000; McIntosh et al., 1995; Stoll et al., 1992a).

Information on the relationship between **infant sex** and hydrocephaly is mixed. Some investigations observed no association (Riley et al., 1998; Stoll et al., 1992a; Buyse, 1990), while other studies reported a predominance among males (Lary and Paulozzi, 2001; Wiswell et al., 1990; Lowry et al., 1986).

Investigations into the relationship between **plurality** and congenital hydrocephaly have produced inconsistent results (Riley et al., 1998; Stoll et al., 1992a; Doyle et al., 1991; Ramos-Arryo, 1991; Kallen, 1986). Hydrocephaly has been associated with lower **birth weight** and **intrauterine growth retardation** (Riley et al., 1998; Mili et al., 1991; Khoury et al., 1988). One investigation reported no statistically significant relationship between hydrocephaly and **macrosomia** (Waller et al., 2001), while another study found increased risk of hydrocephaly with large for gestational age (Lapunzina et al., 2002).

A woman who has had one child with congenital hydrocephaly has a **recurrence risk** of 1-5% of having another affected child. If the hydrocephaly is associated with an inherited disorder, the risk is higher (Schrander-Stumpel and Fryns, 1998; Buyse, 1990). Hydrocephaly rates have been reported to be higher for **consanguineous parents** (Rittler et al., 2001; Rajab et al., 1998; Stoltenberg et al., 1997; Stoll et al., 1992a).

FACTORS IN LIFESTYLE OR ENVIRONMENT

One investigation identified no significant association between **maternal nursing occupation** and hydrocephaly risk (Matte et al., 1993). Another study failed to identify any significant association between hydrocephaly and proximity to various types of **industry** (Castilla et al., 2000). In one investigation, risk of hydrocephaly was significantly increased with high environmental **lead** exposure (Vincenti et al., 2001).

Maternal prenatal **infection** (toxoplasmosis, syphilis, cytomegalovirus, rubella) has been strongly associated with increased hydrocephaly prevalence (Schrander-Stumpel and Fryns, 1998; Stoll et al., 1992a; Vintzileos et al., 1983). One investigation failed to find any effect on hydrocephaly risk for maternal **epilepsy**, **x-rays**, **hypertension**, **fever**, **"flu**," **medication exposure**, or **occupational exposure** (Stoll et al., 1992a). The relationship between maternal **diabetes** and hydrocephaly risk is not clear (Stoll et al., 1992a; Becerra et al., 1990). Another study found no relationship between maternal **hypothyroidism** and hydrocephaly; however, risk of the defect was increased with maternal **hyperthyroidism** (Khoury et al., 1989). Maternal **common cold** in the first trimester of pregnancy has been reported to increase risk of hydrocephaly (Zhang and Cai, 1993).

Maternal **smoking** does not appear to affect hydrocephaly rates (Van Den Eeden et al., 1990). An investigation reported increased risk of hydrocephaly with maternal **oral contraceptive** use, although exposure was reported for only one case (Correy et al., 1991). Another study has found no relationship between **parental occupation of farmer** and hydrocephaly prevalence; however, the study suggested increased hydrocephaly risk with parental **pesticide** exposure (Kristensen et al., 1997). A recent study

reported an increased rate of hydrocephaly among infants born to women with **obesity** but who were not diabetic (Moore et al., 2000). Living in proximity to **hazardous waste sites** has not been found to affect risk of hydrocephaly (Dolk et al., 1998) nor has **paternal ionizing radiation exposure** (Doyle et al., 2000). One study reported no association between hydrocephaly risk and maternal or paternal occupational exposure to **electromagnetic fields**; however, exposure was based on linkage to census data and exposure assessments by an expert panel (Blaasaas et al., 2002). Hydrocephaly does not appear related to **water chlorination** (Kallen and Robert, 2000).

Case reports and a case-control study suggest that risk of hydrocephaly may be increased with maternal use of **misoprostol**, a synthetic prostaglandin used for elective terminations (Orioli and Castilla, 2000). Hydrocephaly has not been associated with maternal use of cough medicines containing **dextromethorphan** (Martinez-Frias and Rodriguez-Pinilla, 2001) the antibiotic **oxytetracycline** (Czeizel and Rockenbauer, 2000), **cephalosporin antibiotics** (Czeizel et al., 2001a), **nalidixic acid** (Czeizel et al., 2001b), ampicillin (Czeizel et al., 2001c), **calcium channel blockers** (Sorensen et al., 2001), or the **benzodiazepines** nitrazepam, medazepam, tofisopam, alprazolum, and clonazepam (Eros et al., 2002). One investigation identified a relationship between maternal **anesthesia** exposure in the first trimester and hydrocephaly, particularly in association with other birth defects (Sylvester et al., 1994).

Several studies have evaluated the relationship between maternal **multivitamin use** and **folic acid** and congenital hydrocephaly risk. The studies found a slight reduction in risk; however, this reduction was not considered significant (Werler et al., 1999; Czeizel et al., 1996; Czeizel, 1993). Furthermore, a study that examined **co-trimoxazole**, a combination of trimethoprim and sulfamethoxazole that is a folic acid antagonist, failed to find any association between the medication and hydrocephaly (Czeizel, 1990).

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Please Note: *The primary purpose of this report is to provide background necessary for conducting cluster investigations. It summarizes literature about risk factors associated with this defect. The strengths and limitations of each reference were not critically examined prior to inclusion in this report. Consumers and professionals using this information are advised to consult the references given for more in-depth information.*

This report is for information purposes only and is not intended to diagnose, cure, mitigate, treat, or prevent disease or other conditions and is not intended to provide a determination or assessment of the state of health. Individuals affected by this condition should consult their physician and when appropriate, seek genetic counseling.